## **CLAIMS**

A compound of formula (I)

$$Ar^{1} - CHCH_{2}NHCR^{4}R^{5}(CH_{2})_{k}$$

$$O(CH_{2})_{m}Z-(CH_{2})_{p}CR^{a}R^{b}$$

$$OH$$

$$(I)$$

or a salt, solvate, or physiologically functional derivative thereof, wherein:

k is an integer of from 1 to 3;

m is an integer of from 2 to 4;

p is an integer of from 0 to 3;

Z is O or CH2-

R¹ is selected from hydrogen, C₁-6alkyl, hydroxy, C₁-6alkoxy, cyano, nitro, halo,

 $C_{1-6}$ haloalkyl,  $XCO_2R^8$ ,  $-XC(O)NR^7R^8$ ,  $-XNR^6C(O)R^7$ ,  $-XNR^6C(O)NR^7R^8$ ,  $-XNR^6C(O)NC(O)NR^7R^8$ ,  $-XNR^6SO_2R^7$ ,  $-XSO_2NR^9R^{10}$ ,  $XSR^6$ ,  $XSOR^6$ ,  $XSO_2R^6$ ,  $XNR^6SO_2NR^7R^8$ ,  $XNR^6SO_2NR^7COOR^7$ ,

-XNR<sup>7</sup>R<sup>8</sup>. -XNR<sup>6</sup>C(O)OR<sup>7</sup>,

or  $R^1$  is selected from -X-aryl, -X-hetaryl, or -X-(aryloxy), each optionally substituted by 1 or 2 groups independently selected from hydroxy,  $C_{1-6}$ alkoxy, halo,  $C_{1-6}$ alkyl,

 $C_{1-6}$ haloalkyl, -NR $^6$ C(O)R $^7$ , SR $^6$ , SOR $^6$ , -SO $_2$ R $^6$ , -SO $_2$ NR $^9$ R $^{10}$ , -CO $_2$ R $^8$ , -N R $^7$ R $^8$ , or hetaryl optionally substituted by 1 or 2 groups independently selected from hydroxy,  $C_{1-6}$ alkoxy, halo,  $C_{1-6}$ alkyl, or  $C_{1-6}$ haloalkyl;

X is  $-(CH_2)_{q}$  or  $C_{2-6}$  alkenylene;

q is an integer from 0 to 6;

 $R^6$  and  $R^7$  are independently selected from hydrogen,  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl, aryl, hetaryl, hetaryl( $C_{1-6}$ alkyl)- and aryl( $C_{1-6}$ alkyl)- and  $R^6$  and  $R^7$  are each independently optionally substituted by 1 or 2 groups independently selected from halo,  $C_{1-6}$ alkyl,

$$\begin{split} &C_{3\text{--}7} \ \text{cycloalkyl}, \ C_{1\text{--}6} \ \text{alkoxy}, \ C_{1\text{--}6} \text{haloalkyl}, \ -\text{NHC}(O)(C_{1\text{--}6} \text{alkyl}), \ -\text{SO}_2(C_{1\text{--}6} \text{alkyl}), \ -\text{SO}_2(\text{aryl}), \\ &-\text{CO}_2\text{H}, \ \text{and} \ -\text{CO}_2(C_{1\text{--}4} \text{alkyl}), \ -\text{NH}_2, \ -\text{NH}(C_{1\text{--}6} \text{alkyl}), \ \text{aryl}(C_{1\text{--}6} \text{alkyl})-, \ \text{aryl}(C_{2\text{--}6} \text{alkyl})-, \ \text{aryl}(C_{2\text{--}6} \text{alkyl})-, \ -\text{NHSO}_2 \text{aryl}, \ -\text{NH}(\text{hetaryl}(C_{1\text{--}6} \text{alkyl}), \ -\text{NHSO}_2 \text{hetaryl}), \end{split}$$

-NHSO<sub>2</sub>(C<sub>1-6</sub>alkyl), -NHC(O)aryl, or -NHC(O)hetaryl:

R<sup>8</sup> is selected from hydrogen, C<sub>1-6</sub>alkyl and C<sub>3-7</sub> cycloalkyl;

or R<sup>7</sup> and R<sup>8</sup>, together with the nitrogen atom to which they are bonded, form a 5-, 6- or 7-membered nitrogen – containing ring;

 $R^9$  and  $R^{10}$  are independently selected from hydrogen,  $C_{1-6}$ alkyl,  $C_{3-7}$ cycloalkyl, aryl, hetaryl, hetaryl( $C_{1-6}$ alkyl)- and aryl( $C_{1-6}$ alkyl)-, or  $R^9$  and  $R^{10}$ , together with the nitrogen to which they are bonded, form a 5-, 6-, or 7- membered nitrogen containing ring; and  $R^9$  and  $R^{10}$  are each optionally substituted by one or two groups independently selected from halo,  $C_{1-6}$ alkyl, and  $C_{3-7}$ cycloalkyl,  $C_{1-6}$ haloalkyl;

 $R^2$  is selected from hydrogen, hydroxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, halo, aryl, aryl( $C_{1-6}$ alkyl)-,  $C_{1-6}$ haloalkoxy, and  $C_{1-6}$ haloalkyl;

 $R^3$  is selected from hydrogen, hydroxy,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkoxy, halo, aryl, aryl( $C_{1-6}$ alkyl)-,  $C_{1-6}$ alkoxy, and  $C_{1-6}$ haloalkoxy, and  $C_{1-6}$ haloalkyl;

R<sup>a</sup> and R<sup>b</sup> are independently selected from hydrogen and C<sub>1-4</sub> alkyl.

 $R^4$  and  $R^5$  are independently selected from hydrogen and  $C_{1-4}$  alkyl with the proviso that the total number of carbon atoms in  $R^4$  and  $R^5$  is not more than 4: and

Ar<sup>1</sup> is a group selected from

$$R^{11}$$
 $R^{12}$ 
 $R^{13}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{14}$ 
 $R^{15}$ 
 $R^{16}$ 
 $R^{17}$ 
 $R^{18}$ 
 $R^{19}$ 
 $R$ 

wherein R<sup>11</sup> represents halogen, -(CH<sub>2</sub>)<sub>n</sub>OR<sup>15</sup>, -NR<sup>15</sup>C(O)R<sup>16</sup>, -NR<sup>15</sup>SO<sub>2</sub>R<sup>16</sup>, -SO<sub>2</sub>NR<sup>15</sup>R<sup>16</sup>, -NR<sup>15</sup>R<sup>16</sup>, -OC(O)R<sup>17</sup> or OC(O)NR<sup>15</sup>R<sup>16</sup>, and R<sup>12</sup> represents hydrogen, halogen or C<sub>1-4</sub> alkyl;

or R<sup>11</sup> represents –NHR<sup>18</sup> and R<sup>12</sup> and –NHR<sup>18</sup> together form a 5- or 6- membered heterocyclic ring;

R<sup>13</sup> represents hydrogen, halogen, –OR<sup>15</sup> or –NR<sup>15</sup>R<sup>16</sup>;

 $R^{14}$  represents hydrogen, halo $C_{1-4}$  alkyl,  $-OR^{15}$ ,  $-NR^{15}$   $R^{16}$ ,  $-OC(O)R^{17}$  or  $OC(O)NR^{15}R^{16}$ ;

 $R^{15}$  and  $R^{16}$  each independently represents hydrogen or  $C_{1-4}$  alkyl, or in the groups  $-NR^{15}R^{16}$ ,  $-SO_2NR^{15}R^{16}$  and  $-OC(O)NR^{15}R^{16}$ ,  $R^{15}$  and  $R^{16}$  independently represent hydrogen or  $C_{1-4}$  alkyl or together with the nitrogen atom to which they are attached form a 5-, 6- or 7-membered nitrogen-containing ring,

 $\mathsf{R}^{17}$  represents an aryl group which may be unsubstituted or substituted by one or more substituents selected from halogen,  $\mathsf{C}_{1\text{-}4}$  alkyl,

hydroxy, C<sub>1-4</sub> alkoxy or halo C<sub>1-4</sub> alkyl; and

n is zero or an integer from 1 to 4; provided that in the group (a), when  $R^{11}$  represents  $-(CH_2)_nOR^{15}$  and n is 1,  $R^{13}$  is not OH.

- 2. A compound according to claim 1 wherein Ar<sup>1</sup> is selected from group (a) or group (b), as defined in claim 1.
- 3. A compound of formula (I) according to claim 2 wherein group (a) is selected from a group of formula (iv) or (xix):

4. A compound of formula (I) according to claim 2 wherein group (b) is a group of formula (iii):

- 5. A compound of formula (I) according to any of claims 1-4 wherein  $R^1$  is selected from hydrogen,  $C_{1-4}$ alkyl, hydroxy, cyano,  $C_{1-6}$ alkoxy, halo,  $XCO_2R^8$ ,  $XNR^6COR^7$ ,  $XCONR^7R^8$ ,  $NR^6C(O)NR^7R^8$ ,  $XSOR^6$ ,  $XNR^6SO_2NR^7R^8$ ,  $XNR^6SO_2NR^7CO_2R^7$  and  $-NR^6SO_2R^7$  wherein  $R^6$  and  $R^7$  are as defined above.
- 6. A compound of formula (I) according to claim 5 wherein  $R^1$  is selected from  $XC(O)NR^7R^8$  or hydrogen.
- 7. A compound of formula (I) according to any of claims 1-6 wherein  $R^2$  and  $R^3$  each represent hydrogen.

8. A compound of formula (I) according to any of claims 1-7 wherein  $R^4$  and  $R^5$  each represent hydrogen.

- 9. A compound of formula (I) according to any of claims 1-8 wherein R<sup>a</sup> and R<sup>b</sup> each represent hydrogen.
- 10. A compound of formula (I) according to claim 1 which is selected from:

3-{[2-(4-{2-[((2R)-2-hydroxy-2-{4-hydroxy-3-

[(methylsulfonyl)amino]phenyl}ethyl)amino]ethyl}phenoxy)ethoxy]methyl}benzamide;

N-{2-hydroxy-5-[(1R)-1-hydroxy-2-({2-[4-(4-

phenylbutoxy)phenyl]ethyl]amino)ethyl]phenyl}methanesulfonamide;

 $N-(5-\{(1R)-2-[(2-\{4-[2-(benzyloxy)ethoxy]phenyl\}ethyl)amino]-1-hydroxyethyl}-2-$ 

hydroxyphenyl)methanesulfonamide;

3-({2-[4-(2-{[(2R)-2-(3-fluoro-4-hydroxyphenyl)-2-

hydroxyethyl]amino}ethyl)phenoxy]ethoxy}methyl)benzamide;

4-{(1R)-2-[(2-{4-[2-(benzyloxy)ethoxy]phenyl}ethyl)amino]-1-hydroxyethyl}-2-fluorophenol;

2-fluoro-4-[(1R)-1-hydroxy-2-({2-[4-(4-phenylbutoxy)phenyl]ethyl}amino)ethyl]phenol;

3-[(2-{4-[2-({2-hydroxy-2-[5-hydroxy-6-(hydroxymethyl)pyridin-2-

yl]ethyl}amino)ethyl]phenoxy}ethoxy)methyl]benzamide;

6-{2-[(2-{4-[2-(benzyloxy)ethoxy]phenyl}ethyl)amino]-1-hydroxyethyl}-2-

(hydroxymethyl)pyridin-3-ol;

2-(hydroxymethyl)-6-[1-hydroxy-2-({2-[4-(4-phenylbutoxy)phenyl]ethyl}amino)ethyl]pyridin-3-ol;

and salts, solvates and physiologically functional derivatives thereof.

- 11. A method for the prophylaxis or treatment of a clinical condition in a mammal, such as a human, for which a selective  $\beta_2$ -adrenoreceptor agonist is indicated, which comprises administration of a therapeutically effective amount of a compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof.
- 12. A compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in medical therapy.

13. A compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in prophylaxis or treatment of a condition for which a selective  $\beta_2$ -adrenoreceptor agonist is indicated.

- 14. A pharmaceutical formulation comprising a compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and a pharmaceutically acceptable carrier or excipient, and optionally one or more other therapeutic ingredients.
- 15. The use of a compound of formula (I), according to any of claims 1-10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof in the manufacture of a medicament for the prophylaxis or treatment of a clinical condition for which a selective  $\beta_2$ -adrenoreceptor agonist is indicated.
- 16. A process for the preparation of a compound of formula (I), according to any of claims 1-10, or a salt, solvate, or physiologically functional derivative thereof, which comprises:
- (a) deprotection of a protected intermediate, for example of formula (II):

$$Ar^{1} - CHCH_{2}NP^{2}CR^{4}R^{5}-(CH_{2})_{k}$$

$$O(CH_{2})_{m}Z-(CH_{2})_{p}CR^{a}R^{b}$$

$$R^{2}$$

$$R^{1}$$

$$R^{3}$$

$$(II)$$

or a salt or solvate thereof, wherein Ar<sup>1</sup>, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>a</sup>, R<sup>b</sup>, R<sup>4</sup>, R<sup>5</sup>, Z, k, m, and p are as defined for the compounds of formula (I), and P<sup>1</sup> and P<sup>2</sup> are each independently either hydrogen or a protecting group provided that at least one of P<sup>1</sup> and P<sup>2</sup> is a protecting group; or

(b) alkylation of an amine of formula (XIII)

$$Ar^{1}$$
 CHCH<sub>2</sub>NP<sup>2</sup>H (XIII)  
OP<sup>1</sup>

wherein  $Ar^1$  is as defined above for compounds of formula (I) and  $P^1$  and  $P^2$  are each independently either hydrogen or a protecting group, with a compound of formula (XIV):

$$L^{1}CR^{4}R^{5}-(CH_{2})_{k}$$

$$Q(CH_{2})_{m}Z-(CH_{2})_{p}CR^{a}R^{b}$$

$$R^{3}$$

$$(XIV)$$

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^a$ ,  $R^b$ , Z, m, and p are as defined for the compound of formula (I) and  $L^1$  is a leaving group;

(c) reacting a compound of formula (XV):

$$Ar^{1}$$
  $CHCH_{2}L^{3}$  (XV)

wherein P<sup>1</sup> and Ar<sup>1</sup> are as hereinbefore defined and L<sup>3</sup> is a leaving group, with an amine of formula (XVI):

$$L^{1}CR^{4}R^{5}-(CH_{2})_{k}$$

$$Q(CH_{2})_{m}Z-(CH_{2})_{p}CR^{a}R^{b}$$

$$R^{3}$$

$$(XIV)$$

wherein  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^4$ ,  $R^5$ ,  $R^a$ ,  $R^b$ , Z k, m, p and  $P^2$  are as hereinbefore defined; or

d) reacting a compound of formula (XIII):

$$Ar^{1}$$
—CHCH<sub>2</sub>NP<sup>2</sup>H (XIII)

as hereinbefore defined.

with a compound of formula (XVII):

$$O = O(CH_2)_m Z - (CH_2)_p CR^a R^b$$

$$R^2 = R^1$$

$$R^3 = R^2$$

$$(XVII)$$

under conditions suitable to effect reductive amination. followed by the following steps in any order:

- (i) optional removal of any protecting groups;
- (ii) optional separation of an enantiomer from a mixture of enantiomers;
- (iii) optional conversion of the product to a corresponding salt, solvate, or physiologically functional derivative thereof.